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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/314,161	05/19/1999	MICHAL EISENBACH-SCHWARTZ	EIS-SCHWARTZ	4767

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EXAMINER	
BUNNER, BRIDGET E	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 07/30/2002 17

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/314,161	EISENBACH-SCHWARTZ ET AL.	
	Examiner	Art Unit	
	Bridget E. Bunner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 May 2002* .

2a)☒ This action is **FINAL**. *I* 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) *3, 9-18, and 20-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,19 and 38-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-40* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of Application, Amendments and/or Claims

The amendment of 06 May 2002 (Paper No. 16) has been entered in full. Claims 1, 4, 16, and 19 are amended and claims 38-40 are added.

This application contains claims 3, 9-15, 17-18, and 20-37 drawn to an invention nonelected without traverse in Paper No. 12 and 14 (25 April 2001 and 14 September 2001, respectively). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim 16 is now directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Claim 16 depends from claim 13, which was withdrawn with traverse in the Office Action of 14 June 2001 (Paper No. 13) because it was drawn to a non-elected invention. In Applicant's response of 06 May 2002 (Paper No. 16), claim 16 was amended to depend from claim 13 and also to recite that a NS-specific antigen or peptide is administered orally.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 16 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Applicant's continued traversal of the Restriction requirement set forth in Paper No. 13 (14 June 2001) appears moot since the restriction requirement was made final in the previous Office Action (Paper No. 15, 05 December 2001). If Applicant wishes to pursue the matter further, a petition should be filed in accordance with 37 CFR 1.144.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-2, 4-8, 19, and 38-40, as they read upon NS-specific activated T cells and injury, are under consideration in the instant application.

Withdrawn Objections and/or Rejections

1. The notification of a defective declaration at pg 3 of the previous Office Action (Paper No. 15, 05 December 2001) is *withdrawn* in view of Applicant's persuasive arguments (Paper No. 16, 06 May 2002).

2. The objections to claims 1, 2, and 19 at pg 4 of the previous Office Action (Paper No. 15, 05 December 2001) is *withdrawn in part* in view of Applicant's claim amendments (Paper No.16, 06 May 2002). Please see section below on Claim Objections.

3. The rejections to claims 1-2, 4-8, 16, and 19 under 35 U.S.C. 112, second paragraph, as set forth at pg 9-10 of the previous Office Action (Paper No. 15, 05 December 2001) are *withdrawn* in view of the amended claims (Paper No. 16, 06 May 2002). See section below on 35 U.S.C. § 112, second paragraph.

Specification

4. The objections to the specification regarding a more descriptive title of the invention is *maintained and held in abeyance* until all other issues are resolved.

Claim Objections

5. The objections to claims 1, 2, 19, and 38-40 regarding the issue that the claims are not limited to the elected species are *maintained and held in abeyance* until allowable subject matter

is identified. The basis for this rejection is set forth for claims 1, 2, and 19 at pg 4 of the previous Office Action (Paper No. 15, 05 December 2001).

Double Patenting

6. The rejections of claims 1-2 and 38-40 under the judicially created doctrine of obviousness-type double patenting at pg 4-6 of the previous Office Action (Paper No. 15, 05 December 2001) is *maintained and held in abeyance* until all other issues are resolved. The basis for this rejection is set forth for claims 1-2 at pages 4-6 of the previous Office Action (Paper No. 15, 05 December 2001).

Claim Rejections - 35 USC § 112

7. Claims 1-2, 4-8, 19, and 38-40 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (i) a method of reducing secondary neuronal degeneration in the central nervous system or peripheral nervous system to ameliorate the degenerative effects of spinal cord injury or blunt trauma comprising administering to an individual in need thereof a composition consisting of activated T cells sensitized to myelin basic protein (MBP) wherein the MBP-activated T cells accumulate at the site of injury to reduce secondary neuronal degeneration, does not reasonably provide enablement for a method of preventing or inhibiting neuronal degeneration in the central nervous system or peripheral nervous system for ameliorating the effects of injury or disease, comprising administering to an individual in need thereof at least one active ingredient selected from the group consisting of NS-specific activate T cells, a NS-specific antigen, a peptide derived from a NS-specific antigen, a nucleotide sequence encoding a NS-specific antigen, and a nucleotide sequence encoding a peptide derived from a NS-specific antigen, thereby causing NS-specific activated T cells to

accumulate at the site of injury and prevent or inhibit neuronal degeneration at that site. The specification is also does not reasonably provide enablement for a method for inhibiting neuronal degeneration in the central nervous system or peripheral nervous system of an individual in need thereof, comprising causing nervous system-specific activated T cells to accumulate at the site of neuronal degeneration in the individual in need thereof, thereby inhibiting neuronal degeneration at that site. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The basis for this rejection is set forth for originally filed claims 1-2, 4-8, 16, and 19 at pg 6-9 of the previous Office Action (Paper No. 15, 05 December 2001).

Applicant's arguments (Paper No. 16, 06 May 2002), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

(i) Applicant asserts that the examiner is incorrect in interpreting the terms "preventing" and "inhibiting" as being synonymous. Applicant indicates that the term "preventing" means that an activity is prevented from occurring, at least to some extent. Applicant states that "inhibiting" means only to restrain or hinder, but not necessarily to completely stop all activity. Applicant contends that if an activity is inhibited, that means it is decreased. Applicant further adds that if an activity is prevented, that means at least some of the activity which would have otherwise occurred is prevented from happening. Applicant emphasizes that "preventing" does not mean that no activity will occur at all. Applicant argues that the claims call for amelioration of a condition, not a complete cure. Applicant states that the examiner's comments about the amount of experimentation necessary to completely prevent neuronal degeneration misses the point as the claims do not require this.

Applicant's arguments have been fully considered but are not found to be persuasive. Applicant's arguments have been fully considered but are not found to be persuasive because it is inappropriate to read limitations into the claims. The claims must independently define the invention for which patent protection is sought. Furthermore, the specification of the instant application does not define the terms "preventing" and "inhibiting". One skilled in the art can interpret the term "preventing" and "inhibiting" to mean that an activity, i.e. neuronal degeneration, will not occur. As mentioned in the previous Office Action (Paper No. 15, 05 December 2001), undue experimentation would be required of the skilled artisan to determine the quantity of any NS-specific activated T cells administered, the best route of administration, the duration of treatment, and any possible side-effects to completely prevent or inhibit neuronal degeneration in the central nervous system or peripheral nervous system. Since the claims read upon that an activity will not occur, a large quantity of experimentation is necessary to completely prevent neuronal degeneration. (Please note that this particular issue of the 35 U.S.C. 112, first paragraph rejection could be overcome by changing the terms "preventing" and "inhibiting" to "reducing".)

(ii) Applicant asserts the examiner's statement that the specification does not teach reducing secondary neuronal degeneration by administration of any other NS-specific activated T cells other than MBP-activated T cell is not entirely correct. Applicant contends that Example 8.2 refers to administration of MOG, another NS-specific antigen which causes NS-specific activated T cells to accumulate at the site of injury. Applicant argues that it was shown to work as well as MBP, and further supports the credibility of the statements in the present specification that any NS-specific antigen will serve to activate the T cells. Applicant submits that it would not

take undue experimentation to determine what other NS-specific antigens could be used to activate T cells as there is no reason for one of ordinary skill in the art reading the specification to believe that any such antigen will not be operable. Applicant indicates that many examples are given at page 31, lines 18-21 of the specification. Applicant states that since the rejection appears to be based on the examiner's holding that the statements in the present specification are incredible, this is really in the nature of a utility rejection. Applicant considers that no experimentation is necessary to practice this invention as all NS-specific antigens would be expected to be operable to activate T cells for use in the present invention.

Applicant's arguments have been fully considered but are not found to be persuasive. It is noted to Applicant that in the Response to Election Requirement of 25 April 2001 (Paper No. 12), Applicant elected Group I, which is drawn to the administration of NS-specific activated T cells. Example 8.1-8.2 of the specification (pg 68-69) refers to the administration of a MOG *protein* to rats, rather than the elected invention of NS-specific activated T cells. Furthermore, although this example does not exemplify the claimed invention, the administration of MOG is not shown in the specification to activate T cells. Undue experimentation would be required of the skilled artisan to sensitize T cells to every nervous system antigen and administer the cells to an individual to reduce any type of neuronal degeneration. As mentioned by Applicant, the specification teaches many NS-specific antigens that could be used to activate T cells, including PLP, MAG, S-100, β-amyloid, Thy-1, P0, P2, and a neurotransmitter receptor. However, according to MPEP § 2164.06, "the guidance and ease in carrying out an assay to achieve the claimed objectives may be an issue to be considered in determining the quantity of experimentation needed. The Applicant's list of NS-specific antigens in the specification is not

adequate guidance, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Additionally, as was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). The present invention is unpredictable and complex wherein one skilled in the art may not necessarily prevent, inhibit, or reduce any kind of neuronal degeneration in the central nervous system or peripheral nervous system comprising administering all types NS-specific activated T cells.

(iii) Applicant asserts that with respect to oral administration, the examiner's attention is invited to Example 9, which shows an experiment involving oral administration. Applicant has amended claim 16 to the administration of peptide, rather than the administration of T cells.

Applicant's arguments have been fully considered but are not found to be persuasive. Again, it is noted that Applicant elected a method that requires the administration of NS-specific activated T cells. Example 9 in the specification of the instant application teaches the oral administration of the MBP peptide, not MBP-activated T cells. It is noted that claim 16 has been withdrawn from consideration because Applicant has amended the claim to depend from a withdrawn claim. However, it is still noted that the specification teaches that MBP-specific activated T cells are administered to an individual intraperitoneally rather than orally. Relevant

literature reports that limited success has been achieved delivering proteins and peptides orally because of: 1) poor intrinsic permeability across intestinal epithelium, 2) susceptibility to enzymatic attack, 3) rapid post-absorptive clearance, and 4) chemical instability (Pettit et al. Trends Biotech 16: 343-349, 1998; see pg 344-345). Therefore, if proteins and peptides are difficult to deliver orally, one skilled in the art would not expect T cells to be successfully delivered orally, particularly since cells are larger than proteins and peptides.

35 USC § 112, second paragraph

8. Claims 38-39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. Claims 38-39 rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the administration of MBP-activated T cells.

Claim Rejections - 35 USC § 102

10. Claims 1, 4-6, 8, and 38-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Popovich et al. (J Neurosci Res 45: 349-363, 1996). The basis for this rejection is set forth at page 11 of the previous Office Action (Paper No. 15, 05 December 2001).

Popovich et al. teach the intravenous administration of myelin basic protein (MBP) activated T cells into naïve recipient rats (pg 353, col 1-2). Popovich et al. also teach that the MBP-activated T cells are T cells from other donor animals (allogeneic). The T cells are cultured with MBP *in vitro* before being injected into the donor animals (pg 353, ¶ 3). Popovich et al. disclose that MBP is an antigenic component of central nervous system myelin and that

when placed in complete Freud's adjuvant, produces an acute or remitting-relapsing paralytic disease, i.e., experimental autoimmune encephalomyelitis (EAE). (pg 352, ¶ 3-4; pg 353, ¶ 3).

Applicant's arguments (Paper No. 16, 06 May 2002), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that claim 1 requires that the T cells be administered to an individual in need of prevention or inhibition of neural degeneration to ameliorate the degenerative effects of injury or disease. Applicant argues that Popovich et al. administers MBP-activated T cells into naïve recipient rats, which have no such injury or disease. Applicant contends the rats of Popovich et al. are not in need of prevention or inhibition or neuronal degeneration, and therefore, the claims cannot be anticipated. Applicant also states that claim 19 has been amended to specify that the activated T cells must be stored in a cell bank of T cells that have been activated against nervous system antigen. Applicant asserts that the cells of Popovich et al. are not stored in a cell bank, and thus claim 19 is not anticipated.

Applicant's arguments have been fully considered but are not found to be persuasive. Specifically, any individual, particularly the rats of Popovich et al., are in need of prevention of neuronal degeneration. As discussed above in the 35 U.S.C. § 112, first paragraph rejection, the term "preventing" in regard to claim 1 could be interpreted by the skilled artisan to mean that neuronal degeneration will not occur in the central or peripheral nervous systems. Therefore, Popovich et al. discloses the intravenous administration of myelin basic protein activated T cells into naïve recipient rats for prevention of neuronal degeneration in the central nervous system and peripheral nervous system.

New Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Popovich et al. (J Neurosci Res 45: 349-363, 1996) in view of Hay, R. (Human Cell 9(3) : 143-152, 1996).

Popovich et al. teach the intravenous administration of myelin basic protein (MBP) activated T cells into naïve recipient rats (pg 353, col 1-2). Popovich et al. also teach that the MBP-activated T cells are T cells from other donor animals (allogeneic). The T cells are cultured with MBP *in vitro* before being injected into the donor animals (pg 353, ¶ 3).

Popovich et al. do not teach storing the MBP-activated T cells in a cell bank for future use.

Hay teaches that national cell banks have been established for the provision of human cells and tissues to clinicians and research scientists (pg 145-149). Hay et al. also teaches that local clinical centers are excellent sources of human cells and tissues (pg 145, ¶ 2).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the nervous system activated T cells as taught by Popovich et al. by storing the cells in a cell bank as taught by Hay et al. The person of ordinary skill in the art would have been motivated to make that modification because the availability of viable human cells and cell lines, along with the pertinent data on the patient donors, is necessary for current transplantation and biomedical research. The person of ordinary skill in the art reasonably would have expected success because other cells were already being stored at the time the invention was made. Therefore, the claimed invention as a whole was clearly *prima facie* obvious over the prior art.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bridget E. Bunner whose telephone number is (703) 305-7148. The examiner can normally be reached on 8:00-5:30 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BEB
Art Unit 1647
July 23, 2002

GARY L. KUNZ
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